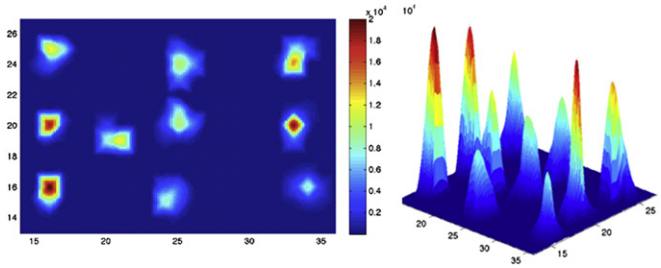
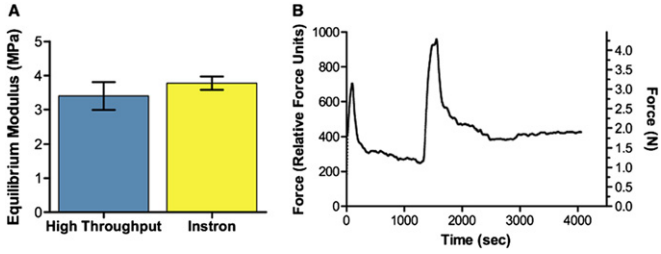
compressive displacement to the HT adapter (Fig 1). Protocol Development: Samples were evaluated by establishing a pre-load to ensure that all indenters were in contact with the IFSR sensor. Subsequently, a nominal 10% compressive strain was applied. With loading, the sensor sampled data at a frequency of 1Hz. Equilibrium force readings were base-lined against the initial force readings; this protocol mitigates the influence of slight differences in sample or indenter heights. Prior to testing, the IFSR sensor was calibrated to ensure accurate conversion of the relative force units outputted to engineering units (Newtons). System Validation and Sample Testing: Multiple polydimethylsiloxane (PDMS) cylinders were tested simultaneously in both the HTMS device and an Instron (with the same testing parameters). To illustrate the capacity of the device to capture time-dependent properties, bovine cartilage cylinders were evaluated by sequential stress-relaxation (5% strain, 20min hold, 10% strain, 40 min hold).

Results: The HTMS testing device accurately captured both equilibrium and dynamic reaction forces from compression of both synthetic and natural materials (Fig 2).



The modulus of PDMS samples tested individually (~3.8 MPa, n=8, Fig 3A) was slightly higher than that found for samples tested simultaneously using the HTMS system (~3.4 MPa, n=8, within ~10% of the individual measures).



As the HTMS will be used for primary screening, slightly lower thresholds for accuracy are acceptable, as secondary screens follow on from 'hits' identified in primary screens. When the device was used to mechanically compress articular cartilage, the IFSR sensor captured the time-dependent stress-relaxation response (Fig 3B).

Discussion: We have developed a HTMS platform for analysis of native and engineered tissues which also can apply a uniform compression force on multiple samples. In this prototype device, transient and equilibrium reaction forces were acquired simultaneously from up to 24 samples and allows for parallel and reliable mechanical evaluation, and in a cost effective manner (~$700). Our current HTMS device evaluates 24 samples at the same time, and is being scaled to accommodate 96- and 384-well plate designs. This validated testing platform will accelerate evaluation of mechanical properties and molecular responses to compressive injury in cartilage tissue engineering, and may help to identify disease-modifying agents in post-traumatic OA.

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DIFFERENCES IN THE OSTEOARTHRITIC SYNOVIAL FLUID COMPOSITION AND RHEOLOGY BETWEEN PATIENTS WITH OR WITHOUT FLARE-UP. A PILOT STUDY

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Purpose: To study the influence of the inflammatory status (flare or not) on hyaluronic acid (HA) and protein composition and on the intrinsic viscosity of the synoviol fluid (SF) from patients with knee osteoarthritis (KOA)

Patients and Methods: Patients with KOA were classified as having flare (F+) when they fulfilled the 4 following clinical criteria: 1) sudden aggravation of knee pain, 2) whose beginning was identifiable, 3) causing nocturnal awakenings 4) with clinical evidence of knee effusion. Patients were classified F- (no flare) if they do not fulfill any of the 3 first criteria. 44 SF were obtained by arthrocentesis and assayed using Steric Exclusion Chromatography, which allows HA to be separated from the proteins and to determine both molecular weight (Mw) and and concentration (C) of both HA and proteins. SF rheology was determined using a rheometer at 25° C using a cone and plate geometry. Steady-state viscosity was determined in Pa.s, as a function of the shear rate at 1s-1. Correlations between Steady-state viscosity(Pa.s) and HA and Pr (Mw, C and Mw x C) were calculated.

Results: Among the 44 assayed SF, 25 were classified F- and 19 F+. There were statistically significant differences between F- and F+ for most of the studied variables: HA concentration and Mw ($p=0.01$ and 0.001 respectively), protein concentration and Mw (p 0.02 and 0.001 respectively), product Mw x C of the proteins ($p<0.0001$) and viscosity($p=0.0005$). The product [(Mw xC) HA x (MwxC) proteins] was highly discriminating between F+ and F- ($p<0.0001$). The steady state viscosity was highly related to HA concentration ($p= 0.0002$) and HA Mw ($p=0.01$) and was negatively correlated with (Mw x C) proteins ($p=0.0005$), protein concentration ($p=0.0007$) and protein Mw ($p=0.03$).

Conclusion This pilot study shows significant differences of SF composition in patients having a flare-up compared to that of patients who do not have flare. These differences relate to both protein and HA composition and suggest that SF analysis makes possible to distinguish patients with and without flare.

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CARTILAGE DAMAGE AFTER ACL RUPTURE; "BARCODE-LIKE LESION" AT THE MEDIAL FEMORAL CONDYLE

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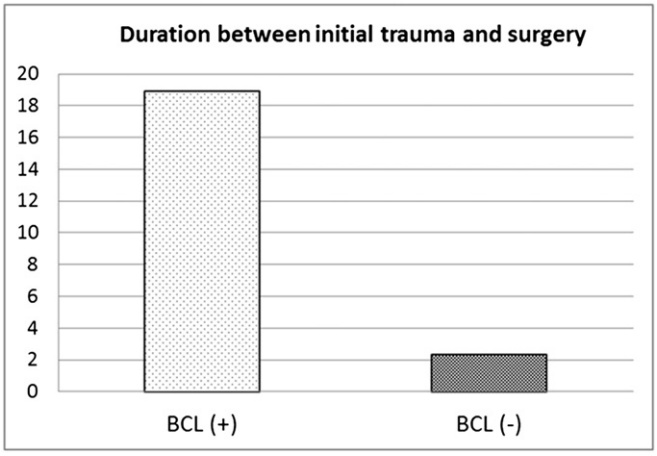
Purpose: This is the first report to identify horizontal articular cartilage fissures at the medial femoral condyle found arthroscopically in ACL-deficient knee, which can be called "Barcode-like lesion (BCL)". The purpose of this study is to describe BCL in details and to find out which factors correlate to its presence.

Methods: 26 cases of primary ACL reconstruction was performed between March and September, 2010. Of these, six were excluded because of lack of precise data, and twenty cases (male 17 knees and female 3 knees) with average age of 22.7±4.5 years old were enrolled in this study. Cases with meniscus tear and Grade-1 MCL injury were included. Cases with PCL and/or postero-lateral corner instability and with Grade-2 or -3 MCL injury were excluded from the study. Medical records were retrospectively reviewed regarding duration between initial trauma and the operation, pre-operative instability (side to side differences), and intraoperative findings (presence of BCL and its number, cartilage damage of tibial side, and presence of meniscal tear).

Results:BCL was found at weight-bearing portion of medial femoral condyle in 11 cases (9 males,2 females)out of 20. The number of BCL includes one in one case, two in seven cases and three in two cases. ICRS grade-IV was found in one case. Duration between initial trauma and the surgery in BCL (+) group was significantly longer than that in BCL (-) group (BCL (+), 18.9±13.3 months; BCL (-), 2.3±0.5 months;P=0.0095). All knees in BCL (-) group had intact medial meniscus, but five out of 11 BCL (+) knees had bucket-handle tear including posterior body of medial meniscus. Cartilage damage at tibial side was none or minimal. There was no difference in pre-operative instability evaluated by Telos-SE between two groups. Lysholm score of each group at one year follow-up did not significantly differ from each other. Second look arthroscopy was done in

three cases from each groups one year after the surgery and revealed that cartilage damage deteriorated in all three cases of BCL (+).
Conclusions: Fleming et al. reported that dGEMRIC index decreased especially at medial femoral condyle after ACL rupture. This means that cartilage compositional change is already there after ACL injury. The present results showed that the longer the interval between the initial traumatic episode and the reconstruction surgery becomes the more likely meniscal damage is, leading to cartilage damage described here as the "Barcode-like lesion" at the medial femoral condyle. This cartilage damage did not essentially improve one year after the surgery.



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PREVALENCE OF IMPINGEMENTS SIGN IN 1992 HIPS FROM THE MROS COHORT: PRELIMINARY RESULTS.

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Background and aims: Femoroacetabular impingement (FAI) is a recently appreciated cause of hip pain and early, rapidly progressive osteoarthritis (OA). The purposes of this study are to evaluate the prevalence of FAI in elderly men and to correlate radiographic FAI with radiographic hip OA and hip pain.
Material and methods: Pelvic radiographs were obtained at visit 2 of MrOS. At this time 1992 hip radiographs have been evaluated. Each hip was assessed for cam type FAI by measurement of the caput-collum-diaphysis (CCD) angle and impingement slope as well as for pincer type FAI by measurement of the impingement angle and lateral center-edge angle (CE). Radiographic hip OA was assessed by expert readers and summary grades (modified Croft) 0-4 were recorded. Pain variables and covariates were collected at study visit 2. Logistic regression was used to evaluate the association of FAI and prevalent radiographic hip OA, adjusted for age, race, and body mass index.
Results: The cohort ages ranged from 69 and 93 years with a mean of 76.5 years. Reliability for radiographic endpoint assessments by Cohen's kappa values for intra-observer agreement on categorical classification was calculated: 0.62, 0.78, 0.84, and 0.86 for impingement slope, impingement angle, CE and CCD angles, respectively. The Cohen's kappa values for inter-observer agreement on categorical classification were 0.60, 0.60, 0.85, and 0.65 for impingement slope, impingement angle, CE and CCD angles, respectively. The prevalence of FAI pincer and cam or mixed types were 37%, 15% and 25%, respectively. The CE angle was greater than 39° in 733 (36.8%) subjects; the CCD angle was less than 125° in 252 (12.7%) subjects; the impingement angle was less than 70° in 293 (14.7%) subjects and Tonnis' angle less than 0° in 504 (25.3%) subjects. The prevalence of hip OA by Croft score was distributed as follows: 1543 (77.5%), 335 (16.8%), 56 (2.8%), 18 (0.9%), 7 (0.4%) for grade 0 to 4, respectively. Both the prevalence of radiographic hip OA and severity of OA were higher in patients with radiographic evidence of FAI compared to patients without signs of FAI: CE $> 39°$ (OR = 1.46, $p<0.0001$), CCD $< 125°$, (OR= 1.79, p= 0.0002) and Tonnis' angles $< 0°$ (OR = 1.77, $p <0.0001$). These associations remained significant after adjustment for age, race, and body mass index. No significant correlation was found for the impingement angle in either radiographic hip OA or pain. Also, there was no correlation with the individual FAI parameters and hip pain.
Discussion: FAI is prevalent in elderly men and is associated with radiographic hip OA. We determined that the radiographic criteria for the pincer type of FAI is associated with the prevalence and severity of hip OA, and that the CCD angle is associated with radiographic hip OA.

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LARGE-SCALE ANALYSIS OF THE TRANSCRIPTIONAL RESPONSE OF CHONDROCYTES TO MECHANICAL STRESS

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Purpose: Mechanical stress (stretch) is one of the main actors of cartilage homeostasis and osteoarthritis pathogenesis. Little is known about the underlying molecular mechanisms involved in the response of articular chondrocytes to mechanical stress. Several studies have described the precise signaling pathways of stretch stress applied on chondrocytes, but they focused on only a few previously chosen molecular targets. We aimed to screen, using a large-scale approach, the global gene expression profiles of articular chondrocytes submitted to stretch stress.
Methods: Primary rabbit articular chondrocytes from 4-week-old female New Zealand white rabbits cultured in monolayer at high density were subjected or not to equibiaxial stretching (5%, 1 Hz) for 20 hours, applied by using the Flexcell® system (FX-3000™) and total RNA was extracted. Seven independent experiments were done. RNA from stretched and static chondrocytes underwent microarray assay using Rabbit Genome Oligonucleotides Micro-arrays 4X44K (Agilent Technologies). A gene was considered differentially regulated between stretch and static conditions if the ratio between these two conditions was more than two-fold with a *P* value less than 0.05 (n=7). Gene expression was also examined by real-time quantitative RT-PCR and protein expression by western blot analysis.
Results: We identified 95 up-regulated genes and 169 down-regulated genes in response to stretch stress, among which 31 and 50, respectively, were known genes in the rabbit genome. Eight of the up-regulated genes and eleven of the down-regulated genes showed greater than four-fold change in expression between stretch and static conditions. The validity of our micro-array analysis was confirmed by qRT-PCR and western blot. Some of the modulated genes are involved in inflammation, cell death and extracellular matrix degradation in normal and osteoarthritis cartilage, so their modulation by mechanical stress was not surprising. However, some identified targets with unknown function in cartilage may have a role in cartilage homeostasis and osteoarthritis pathogenesis.
Conclusions: Large-scale analysis of the transcriptional response of chondrocytes to mechanical stretch stress highlighted new molecules possibly implicated in osteoarthritis pathogenesis.

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LOW-INTENSITY PULSED ULTRASOUND INHIBITS MESSENGER RNA EXPRESSION OF MATRIX METALLOPROTEINASE-13 INDUCED BY INTERLEUKIN-1 βETA IN INTENSITY-DEPENDENT MANNER ON CHONDROCYTES

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Purpose: Low-intensity pulsed ultrasound (LIPUS) has been studied about its ability which promotes anabolic reactions like collagen and aggrecan synthesis on the articular cartilage. However, it is still unknown about the effective intensity of LIPUS on articular cartilage degradation factors, and the effect of LIPUS on the articular cartilage with the inflammatory symptoms of several levels. The purpose of this study is to investigate the immediate effect of LIPUS using several intensities on chondrocytes accompanied by the inflammatory reaction induced by IL-1β.
Methods: Chondrocytes were aseptically isolated from rat knee joints (Wistar, 12 week-old). All procedures were approved from Institutional Animal Care and Use Committee in Kyoto University (Kyoto, Japan). After